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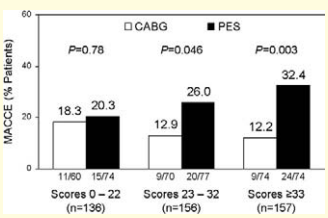
Inside This Issue

STATE-OF-THE-ART PAPER

CLINICAL RESEARCH



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INTERVENTIONAL CARDIOLOGY

TAVI for Patients at Very High or Prohibitive Surgical Risk 1080

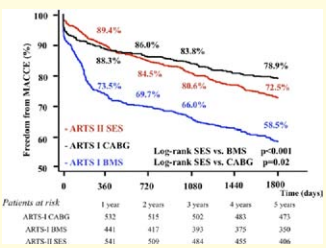
Josep Rodés-Cabau, John G. Webb, Anson Cheung, Jian Ye, Eric Dumont, Chris Feindel, Mark Osten, Madhu K. Natarajan, James L. Velianou, Giuseppe Martucci, Benoît DeVarennes, Robert Chisholm, Mark D. Peterson, Samuel V. Lichtenstein, Fabian Nietlispach, Daniel Doyle, Robert DeLarochellière, Kevin Teoh, Victor Chu, Adrian Dancea, Kevin Lachapelle, Asim Cheema, David Latter, Eric Horlick

Rodés-Cabau and colleagues evaluated the acute and late outcomes of patients in a comprehensive transcatheter aortic valve implantation (TAVI) program including both the transfemoral (TF) and transapical (TA) approaches for patients considered inoperable or at very high surgical risk. A total of 345 procedures (TF: 168, TA: 177) were performed. The procedure was successful in 93% of the cases, and procedural and 30-day mortality were 1.7% and 10.4%, respectively. After a median follow-up of 8 months, the cumulative mortality rate was 22%. This TAVI program which includes both TF and TA approaches resulted in mortality comparable to that predicted by surgical risk calculators.

Editorial Comment: Bernard Iung, Dominique Himbert, Alec Vahanian, p. 1091

INTERVENTIONAL CARDIOLOGY

5-Year Outcomes of ARTS II: SES Compared to CABG and BMS in Subjects With Multivessel Disease 1093



Patrick W. Serruys, Yoshinobu Onuma, Scot Garg, Pascal Vranckx, Bernard De Bruyne, Marie-Claude Morice, Antonio Colombo, Carlos Macaya, Gert Richardt, Jean Fajadet, Christian Hamm, Monique Schuijer, Tessa Rademaker, Kristel Wittebols, Hans Peter Stoll, on behalf of the ARTS II Investigators

Serruys and colleagues compared the 5-year clinical outcomes of sirolimus-eluting stents (SES) in the ARTS II (Arterial Revascularization Therapies Study II) with the outcomes of coronary artery bypass graft (CABG) and bare-metal stenting (BMS) from the ARTS I. ARTS I was a randomized trial of 1,205 patients with multivessel disease comparing CABG and BMS, while the ARTS II was a nonrandomized trial of 607 patients using SES and the same inclusion and exclusion criteria, end points, and protocol definitions. At 5-year follow-up, the death/cerebrovascular accident/myocardial infarction event-free survival rate was 92% in ARTS II SES, versus 89% and 87% in the ARTS I CABG and BMS cohorts, respectively. Freedom from revascularization in the ARTS II SES cohort was lower than in ARTS I CABG, but higher than in ARTS I BMS. The cumulative incidence of definite stent thrombosis was 3.8% in ARTS II SES. At 5 years, SES had a safety record comparable to CABG and superior to BMS; approximately one-third of the events seen with SES may be related to stent thrombosis.

(continued on page A-24)

BIOMARKERS

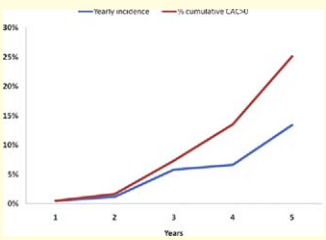
Myeloperoxidase and CRP Predict Cardiovascular Mortality **1102**

Claire L. Heslop, Jiri J. Frohlich, John S. Hill

Heslop and colleagues evaluated the relative and combined value of oxidative stress biomarkers for predicting cardiovascular mortality. Myeloperoxidase (MPO), nitrotyrosine, oxidized low-density lipoprotein, and C-reactive protein (CRP) were measured in a prospective cohort of 885 subjects who underwent selective coronary angiography. During 13 years of follow-up, MPO independently predicted coronary artery disease, and top tertile MPO levels predicted a 2.4-fold risk of cardiovascular mortality, compared to patients with the lowest tertile MPO levels. Patients with elevated MPO or CRP levels had 5.3-fold higher cardiovascular mortality risk; patients with high levels of both had a 4.3-fold higher risk compared to those with only 1 elevated marker. Measuring MPO and CRP together may improve long-term cardiac risk assessment.

CARDIAC IMAGING

What Is the "Warranty Period" for a Normal CAC Scan? **1110**



James K. Min, Fay Y. Lin, David S. Gidseg, Jonathan W. Weinsaft, Daniel S. Berman, Leslee J. Shaw, Alan Rozanski, Tracy Q. Callister

A coronary artery calcium (CAC) scan can identify the presence or absence of atherosclerosis, but little is known regarding the temporal "warranty period" of a normal scan. Min and colleagues assessed the frequency of progression and time to progression of CAC in 422 patients with no baseline CAC (CAC = 0). All subjects underwent annual CAC scanning for 5 consecutive years. One-fourth of subjects developed CAC during follow-up. The incidence of conversion to CAC >0 was nonlinear and was highest in the fifth year. Among patients with a normal baseline CAC scan, the rate of conversion to an abnormal CAC scan occurs at a low frequency before 4 years of follow-up.

Editorial Comment: Harvey S. Hecht, p. 1118

PEDIATRIC CARDIOLOGY

Efficacy and Safety of Rosuvastatin for Children With Familial Hypercholesterolemia **1121**

Hans J. Avis, Barbara A. Hutten, Claude Gagné, Gisle Langslet, Brian W. McCrindle, Albert Wiegman, Judith Hsia, John J. P. Kastelein, Evan A. Stein

Avis and colleagues evaluated the efficacy and safety of rosuvastatin in children with familial hypercholesterolemia (FH). This study comprised a 12-week, double-blind, randomized, placebo-controlled trial, followed by a 40-week, open-label, titration-to-goal extension phase in children, age 10 to 17 years, with FH. Compared with placebo, rosuvastatin 5, 10, and 20 mg reduced low-density lipoprotein cholesterol (LDL-C) by 38%, 45%, and 50%, respectively. With a maximum allowed dose of 20 mg, 40% achieved the treatment goal of <110 mg/dl. While some patients had a transient elevation in liver enzymes and creatine kinase, all resolved with either continued treatment or rechallenge. Rosuvastatin 20 mg daily can safely reduce LDL-C by ~50% in children with FH.

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HYPERTROPHIC CARDIOMYOPATHY

Mutations in ACTN2 Can Cause HCM 1127

Christine Chiu, Richard D. Bagnall, Jodie Ingles, Laura Yeates, Marina Kennerson, Jennifer A. Donald, Mika Jormakka, Joanne M. Lind, Christopher Semsarian

Studies have shown that hypertrophic cardiomyopathy (HCM) can be caused by one of over 450 different mutations in at least 13 different genes. However, only 50% of HCM patients have one of the identified mutations. Chiu and colleagues performed a genome-wide linkage analysis on a family of 23 subjects with familial HCM. This suggested a mutation in the area of the alpha-actinin-2 (ACTN2) gene and further testing confirmed this. This gene was then analyzed in another 297 HCM probands and 3 other causative ACTN2 mutations were identified. This is the first genome-wide linkage analysis that shows mutations in ACTN2 cause HCM.

Editorial Comment: J. Martijn Bos, Michael J. Ackerman, p. 1136

PLATELETS AND THROMBOSIS

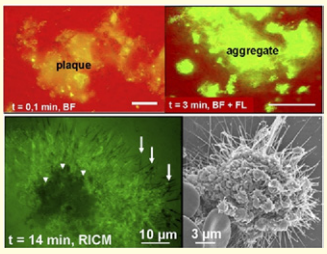
Less Platelet Inhibition With Dual Antiplatelet Therapy in Diabetics With Kidney Disease 1139

Dominick J. Angiolillo, Esther Bernardo, Davide Capodanno, David Vivas, Manel Sabaté, José Luis Ferreiro, Masafumi Ueno, Pilar Jimenez-Quevedo, Fernando Alfonso, Theodore A. Bass, Carlos Macaya, Antonio Fernandez-Ortiz

Angiolillo and colleagues measured the impact of renal function on platelet reactivity in patients with diabetes mellitus (DM). This was a cross-sectional, observational study in which patients with DM on maintenance aspirin and clopidogrel therapy were studied for the degree of platelet inhibition. Patients with moderate/severe chronic kidney disease (CKD) (GFR <60 ml/min) had significantly higher adenosine diphosphate- and collagen-induced platelet aggregation compared to those without CKD. After adjustment for potential confounders, patients with moderate/severe CKD were 2.4 to 3.8 times more likely to have high platelet reactivity. In DM patients, impaired renal function is associated with reduced clopidogrel-induced antiplatelet effects.

PLATELETS AND THROMBOSIS

Arterial Thrombus Formation on Atherosclerotic Plaques Requires 2 Steps 1147



Armin J. Reininger, Isabell Bernlochner, Sandra M. Penz, Catherine Ravanat, Peter Smethurst, Richard W. Farndale, Christian Gachet, Richard Brandl, Wolfgang Siess

Reininger and colleagues studied the initial mechanism of arterial thrombus formation induced by atherosclerotic plaques. Human atheromatous plaque material, obtained from carotid endarterectomy samples, was exposed to blood or blood components. Platelet aggregation and coagulation were measured under static and arterial flow conditions by microscopic and physiological techniques. Thrombus formation was found to occur in 2 discrete steps. The rapid first phase was triggered by platelet glycoprotein VI adhesion onto plaque collagen. The second phase of coagulation started after a delay of >3 min with the binding of thrombin and fibrin to the activated platelets, and was driven entirely by plaque tissue factor (TF). Coagulation occurred only in flow niches, with no evidence for a role of blood-borne TF.